

PABST PATENT GROUP

RECEIVED  
CENTRAL FAX CENTER

FEB 15 2005

Pabst Patent Group LLP  
 400 Colony Square, Suite 1200  
 1201 Peachtree Street  
 Atlanta, GA 30361  
 Telephone (404) 879-2150  
 Telefax (404) 879-2160  
 information@pabstpatent.com  
 www.pabstpatent.com

**TELEFAX****Date:** February 15, 2005**Total pages:** 20  
(including cover sheet)**To:** US PTO**Telephone:** **Telefax:** 703-872-9306**From:** Patrea L. Pabst**Telephone:** 404-879-2151 **Telefax:** 404-879-2160**Our Docket No.** PDC 119**Client/Matter No.** 078374-00011**Your Docket No.****Please call (404) 879-2150 if you did not receive all of the pages, or if they are illegible.**

**CONFIDENTIALITY NOTICE:** This facsimile, along with any documents, files, or attachments, may contain information that is confidential, privileged, or otherwise exempt from disclosure. If you are not the intended recipient or a person responsible for delivering it to the intended recipient, you are hereby notified that any disclosure, copying, printing, distribution or use of any information contained in or attached to this facsimile is strictly prohibited. If you have received this facsimile in error, please immediately notify us by facsimile or by telephone collect at the numbers stated above, and destroy the original facsimile and its attachments without reading, printing, or saving in any manner. Your cooperation is appreciated. Thank you.

**MESSAGE:****REPLACEMENT FOR APPEAL BRIEF**  
**FAXED EARLIER TODAY****IN THE UNITED STATES PATENT AND TRADEMARK OFFICE****Applicants:** Solomon S. Steiner and Bryan R. Wilson**Serial No.:** 09/766,362      **Art Unit:** 1615**Filed:** January 19, 2001      **Examiner:** Humera Sheikh**For:** *DRY POWDER FORMULATIONS OF ANTIHISTAMINE FOR  
NASAL ADMINISTRATION***Attached Items:**

Transmittal Form PTO/SB/21; Fee Transmittal Form PTO/SB/17;  
 Appeal Brief with Appendix; Authorization to charge Deposit Account No. 50-3129;  
 Certificate of Fax Transfer

(45048198.1)

PTO/SB/21 (09-04)

Approved for use through 07/31/2008, OMB 0651-0031  
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

**TRANSMITTAL  
FORM**

(to be used for all correspondence after initial filing)

Application Number	09/766,362
Filing Date	January 19, 2001
First Named Inventor	Solomon S. Steiner
Art Unit	1615
Examiner Name	Humera Sheikh
Total Number of Pages in This Submission	PDC 119

FEB 15 2005

**RECEIVED****CENTRAL FAX CENTER****ENCLOSURES (Check all that apply)**

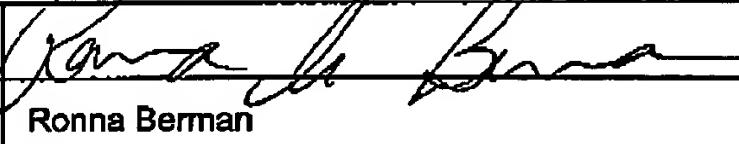
<input checked="" type="checkbox"/> Fee Transmittal Form	<input type="checkbox"/> Drawing(s)	<input type="checkbox"/> After Allowance Communication to TC
<input type="checkbox"/> Fee Attached	<input type="checkbox"/> Licensing-related Papers	<input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences
<input type="checkbox"/> Amendment/Reply	<input type="checkbox"/> Petition	<input checked="" type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief)
<input type="checkbox"/> After Final	<input type="checkbox"/> Petition to Convert to a Provisional Application	<input type="checkbox"/> Proprietary Information
<input type="checkbox"/> Affidavits/declaration(s)	<input type="checkbox"/> Power of Attorney, Revocation	<input type="checkbox"/> Status Letter
<input type="checkbox"/> Extension of Time Request	<input type="checkbox"/> Change of Correspondence Address	<input type="checkbox"/> Other Enclosure(s) (please identify below):
<input type="checkbox"/> Express Abandonment Request	<input type="checkbox"/> Terminal Disclaimer	
<input type="checkbox"/> Information Disclosure Statement	<input type="checkbox"/> Request for Refund	
<input type="checkbox"/> Certified Copy of Priority Document(s)	<input type="checkbox"/> CD, Number of CD(s) _____	
<input type="checkbox"/> Reply to Missing Parts/ Incomplete Application	<input type="checkbox"/> Landscape Table on CD	
<input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.52 or 1.53		
<b>Remarks</b>		

**SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT**

Firm Name	Pabst Patent Group LLP		
Signature			
Printed name	Patrea L. Pabst		
Date	February 15, 2005	Reg. No.	31,284

**CERTIFICATE OF TRANSMISSION/MAILING**

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below:

Signature			
Typed or printed name	Ronna Berman	Date	February 15, 2005

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

PTO/SB/17 (12-04)

Approved for use through 07/31/2008. OMB 0651-0032

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995 no persons are required to respond to a collection of information unless it displays a valid OMB control number

<b>Effective on 12/08/2004.</b> <b>Fees pursuant to the Consolidated Appropriations Act, 2005 (H.R. 4918).</b> <b>FEE TRANSMITTAL</b> <b>For FY 2005</b>		<b>Complete if Known</b>	
		Application Number	09/766,362
		Filing Date	January 19, 2001
		First Named Inventor	Solomon S. Steiner
		Examiner Name	Hurnera Sheikh
		Art Unit	1615
TOTAL AMOUNT OF PAYMENT	(\$250.00)	Attorney Docket No.	PDC 119

**METHOD OF PAYMENT (check all that apply)**

<input type="checkbox"/> Check	<input type="checkbox"/> Credit Card	<input type="checkbox"/> Money Order	<input type="checkbox"/> None	<input type="checkbox"/> Other (please identify): _____
<input checked="" type="checkbox"/> Deposit Account Deposit Account Number: 50-3129 Deposit Account Name: Pabst Patent Group LLP				

For the above-identified deposit account, the Director is hereby authorized to: (check all that apply)

<input checked="" type="checkbox"/> Charge fee(s) indicated below	<input type="checkbox"/> Charge fee(s) indicated below, except for the filing fee
<input checked="" type="checkbox"/> Charge any additional fee(s) or underpayments of fee(s) under 37 CFR 1.16 and 1.17	<input checked="" type="checkbox"/> Credit any overpayments

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

**FEE CALCULATION****1. BASIC FILING, SEARCH, AND EXAMINATION FEES**

<u>Application Type</u>	<u>FILING FEES</u>		<u>SEARCH FEES</u>		<u>EXAMINATION FEES</u>		<u>Fees Paid (\$)</u>
	<u>Fee (\$)</u>	<u>Small Entity Fee (\$)</u>	<u>Fee (\$)</u>	<u>Small Entity Fee (\$)</u>	<u>Fee (\$)</u>	<u>Small Entity Fee (\$)</u>	
Utility	300	150	500	250	200	100	
Design	200	100	100	50	130	65	
Plant	200	100	300	150	160	80	
Reissue	300	150	500	250	600	300	
Provisional	200	100	0	0	0	0	

**2. EXCESS CLAIM FEES**

<u>Fee Description</u>	<u>Small Entity</u>
Each claim over 20 or, for Reissues, each claim over 20 and more than in the original patent	50 25
Each independent claim over 3 or, for Reissues, each independent claim more than in the original patent	200 100
Multiple dependent claims	360 180

<u>Total Claims</u>	<u>Extra Claims</u>	<u>Fee (\$)</u>	<u>Fee Paid (\$)</u>	<u>Multiple Dependent Claims</u>	<u>Fee (\$)</u>	<u>Fee Paid (\$)</u>
18 - 20 or HP = 0	x	=				
HP = highest number of total claims paid for, if greater than 20						

<u>Indep. Claims</u>	<u>Extra Claims</u>	<u>Fee (\$)</u>	<u>Fee Paid (\$)</u>	<u>Fee (\$)</u>	<u>Fee Paid (\$)</u>
3 - 3 or HP = 0	x	=			

HP = highest number of independent claims paid for, if greater than 3

**3. APPLICATION SIZE FEE**

If the specification and drawings exceed 100 sheets of paper, the application size fee due is \$250 (\$125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

<u>Total Sheets</u>	<u>Extra Sheets</u>	<u>Number of each additional 50 or fraction thereof</u>	<u>Fee (\$)</u>	<u>Fee Paid (\$)</u>
- 100 =	/ 50 =	(round up to a whole number)	x	=

**4. OTHER FEE(S)**

Non-English Specification, \$130 fee (no small entity discount)

Other: Appeal Brief Filing Fee (small entity) \$250.00

<b>SUBMITTED BY</b>		<b>Registration No.</b> (Attorney/Agent) 31,284	<b>Telephone</b> (404) 879-2151
Signature			
Name (Print/Type)	Patrea L. Pabst		
		Date	February 15, 2005

This collection of information is required by 37 CFR 1.136. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 30 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

PDC 119 / 078374-00011

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Appellant: Solomon S. Steiner and Bryan R. Wilson

**RECEIVED  
CENTRAL FAX CENTER**

Serial No.: 09/766,362

Art Unit: 1615

**FEB 15 2005**

Filed: January 19, 2001

Examiner: Humera Sheikh

For: ***DRY POWDER FORMULATIONS OF ANTIHISTAMINE FOR NASAL ADMINISTRATION***

Mail Stop Appeal Brief-Patents  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**SUBSTITUTE APPEAL BRIEF**

Sir:

Please substitute this Appeal Brief for the one faxed February 15, 2005 at 10:21 a.m. This is an appeal from the final rejection of claims 1-5, 7-12, 14-18, 20 and 21 in the Office Action mailed July 15, 2004, in the above-identified patent application. A Notice of Appeal was filed on December 15, 2004. The Commissioner is hereby authorized to charge \$250.00, the fee for the filing of this Appeal Brief for a small entity, to Deposit Account No. 50-3129. It is believed that no additional fee is required with this submission. However, should an additional fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-3129.

U.S.S.N.: 09/766,362  
Filed: January 19, 2001  
**APPEAL BRIEF**

**(1) REAL PARTY IN INTEREST**

The real party in interest of this application is the assignee, MannKind Corporation.

**(2) RELATED APPEALS AND INTERFERENCES**

There are no related appeals or interferences known to appellant, the undersigned, or appellant's assignee which directly affects, which would be directly affected by, or which would have a bearing on the Board's decision in this appeal.

**(3) STATUS OF CLAIMS ON APPEAL**

Claims 1-5, 7-12, 14-18, 20 and 21 are pending and on appeal. Claims 6, 13, and 19 were cancelled in an Amendment filed August 21, 2003. New claims 20 and 21 were added in an Amendment filed April 12, 2004. The text of each claim on appeal, as pending, is set forth in an Appendix to this Appeal Brief.

**(4) STATUS OF AMENDMENTS**

An amendment after final rejection was filed on October 13, 2004. In the Advisory Action mailed December 7, 2004, the Examiner indicated that this amendment would not be entered. The claims were last amended in the amendment filed April 12, 2004. An appendix sets forth the claims on appeal.

**(5) SUMMARY OF THE INVENTION**

The claims define dry powder formulations suitable for nasal administration that minimize or eliminate systemic side effects (page 2, lines 2-4). The claims also define a drug

U.S.S.N.: 09/766,362  
Filed: January 19, 2001  
**APPEAL BRIEF**

delivery device for nasal administration of the dry powder formulations and a method of administering the dry powder formulations to the nasal region of a patient in need thereof (page 13, lines 3-11). The dry powder formulations reduce the systemic side effects of liquid nasal sprays because the drug is maintained in the nasal cavity (page 2, lines 2-3) due to the selection of microparticles having an average particle size of between 10 and 20 microns formed of drug and dikelopiperazines (page 3, lines 5-10).

#### **(6) ISSUES ON APPEAL**

The issues presented on appeal are:

(1) whether claims 1, 2, 4, 5, 7, 9, 12, 14, 15, 17, and 18 are non-obvious as required by 35 U.S.C. § 103(a) over U.S. Patent No. 5,503,852 to Steiner *et al.* ("Steiner").  
and (2) whether claims 3, 8, 10, 16, 20, and 21 are non-obvious as required by 35 U.S.C. § 103(a) over Steiner in view of U.S. Patent No. 5,690,954 to Illum ("Illum").

#### **(7) GROUPING OF CLAIMS**

The claims do not stand or fall together. Arguments for the separate patentability of the claims are provided below.

#### **(8) ARGUMENTS**

##### **(a) The Invention**

Current administration of antihistamines via intranasal routes in aqueous solution imparts systemic side effects such as somnolence and long lasting, bitter tastes (page 1, lines 13-20). Liquid nasal sprays result in antihistamine penetration into the back of the throat where the

U.S.S.N.: 09/766,362  
Filed: January 19, 2001  
**APPEAL BRIEF**

antihistamine may be orally absorbed and contribute to the central nervous system effects of somnolence and the bitter taste experienced by patients (page 1, lines 17-20). The dry powder formulations reduce the systemic side effects of liquid nasal sprays because the drug is maintained in the nasal cavity (page 2, lines 2-3). This is achieved through the selection of microparticles having an average particle size of between 10 and 20 microns formed of drug and diketopiperazines (page 3, lines 5-10) which are retained in the nasal region and not passed into the pulmonary system or the mouth. Particles smaller than 10 microns could cause the composition to pass into the pulmonary region or mouth, resulting in a less efficient delivery of the drug and causing undesirable side effects with certain type of drugs, e.g., bitterness in the case of an antihistamine. In addition, since the particles as defined by the claims are retained in the nasal region, lower doses of drug can be administered (page 2, lines 23-26).

**(b) Rejections Under 35 U.S.C. § 103**

***The Legal Standard***

As stated in MPEP § 2141, when applying 35 U.S.C. § 103, the following tenets of patent law must be adhered to:

- (A) The claimed invention must be considered as a whole;
- (B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination;
- (C) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and

U.S.S.N.: 09/766,362  
Filed: January 19, 2001  
**APPEAL BRIEF**

(D) Reasonable expectation of success is the standard with which obviousness is determined (MPEP § 2141 citing *Hodosh v. Block Drug Co., Inc.*, 786 F.2d 1136, 1143 n.5, 229 USPQ 182, 187 n.5 (Fed. Cir. 1986)). As noted in Gillette, "Focusing on the obviousness of substitutions and differences, instead of on the invention as a whole, is a legally improper way to simplify the often difficult determination of obviousness." (*Gillette Co. v. S.C. Johnson & Sons, Inc.*, 919 F.2d 720, 724, 16 U.S.P.Q.2d 1923 (Fed. Cir. 1990)).

In rejecting a claim under 35 U.S.C. § 103, the Examiner must establish a *prima facie* case that: (i) the prior art suggests the claimed invention; and (ii) the prior art indicates that the invention would have a reasonable likelihood of success (*In re Dow Chemical Company*, 837 F.2d 469, 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988)). Claims are not *prima facie* obvious if the primary references do not suggest all elements of the claimed invention and the prior art does not suggest the modifications that would bring the primary references into conformity with the application claims (*In re Fritch*, 23 U.S.P.Q.2d, 1780 (Fed. Cir. 1992). *In re Laskowski*, 871 F.2d 115 (Fed. Cir. 1989)). This is not possible when the claimed invention achieves more than what any or all of the prior art references allegedly suggest, expressly or by reasonable implication. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on the applicant's disclosure (*In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)). The MPEP explains that "[t]he mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combinations"

U.S.S.N.: 09/766,362  
Filed: January 19, 2001  
**APPEAL BRIEF**

(MPEP § 2143.01, quoting *In re Mills*, 916 F.2d 680, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990)). The Court of Appeals for the Federal Circuit warned that “the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for showing of the teaching or motivation to combine prior art references” (*In re Dembicza*k , 175 F.3d 994 at 999 (Fed. Cir. 1999)). The “question is whether there is something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination (*WMS Gaming, Inc. v International Game Technology*, 184 F.3d 1339 at 1355 (Fed. Cir. 1999)). “[T]he showing must be clear and particular” (*In re Dembicza*k , 175 F.3d 994 at 999 (Fed. Cir. 1999)). The references themselves must lead those in the art to what is claimed. In this case, there is simply no such teaching.

(i) Rejection of claims 1, 2, 4, 5, 7, 9, 12, 14, 15, 17, and 18 under 35 U.S.C. § 103(a) as obvious over U.S. Patent No. 5,503,852 to Steiner et al. (“Steiner”)

Steiner

Steiner discloses drug delivery systems suitable for oral or intravenous administration wherein diketopiperazines and their analogs form particles incorporating a drug to be delivered. Steiner discloses drugs that are to be released in the circulatory system following injection or after transport from the gastrointestinal (GI) tract following oral delivery (column 10, lines 29-31). Steiner describes formulations that are stable in the blood, stomach, or small intestine (column 11, lines 15-49).

U.S.S.N.: 09/766,362  
Filed: January 19, 2001  
**APPEAL BRIEF**

**Steiner does not disclose drug delivery systems in a form suitable for nasal administration.** Steiner discloses formulations administered in a solution or in the form of a tablet. **Steiner does not disclose dry powder formulations.**

**Steiner does not mention nor suggest a composition of microparticles having an average size between 10 and 20 microns.** In contrast, Steiner discloses administering smaller microparticles, with average diameters between 0.1 and 10 microns for oral or intravenous delivery. (col. 4, lines 32-40). This size range is ineffective for improving the nasal administration of drugs. Microspheres below 10 microns will pass into the pulmonary region or mouth, resulting in a less efficient delivery of the drug and cause undesirable side effects with certain type of drugs, e.g., bitterness in the case of an antihistamine. Thus, Steiner does not address any problems associated with nasal administration of drugs.

Steiner teaches away from nasal drug delivery which requires adhesion to and uptake within the nasal region. Steiner mentions that the microparticles can include a diagnostic imaging agent useful for imaging the nasal tract. However, these microparticles are administered orally or through a needle for intravenous administration (col. 13, lines 14-24 and col. 11, line 65 until col. 12, line 4 and col. 12, lines 20-22), not via inhalation. Imaging the nasal tract is very different from drug delivery through the nasal mucosa. In diagnostic imaging, the imaging agent is administered orally or intravenously and travels through the body emitting signals that are recorded and transformed into a desired "image", while in nasal drug delivery the drug is absorbed through the nasal mucosa where it acts locally, and may also be distributed

U.S.S.N.: 09/766,362  
Filed: January 19, 2001  
**APPEAL BRIEF**

systemically in the body. Formulations which are suitable for injection are administered in solution, in a volume that suspends the particles so that they are readily distributed at the site of administration. In contrast, a formulation suitable for nasal administration cannot be suspended in a quantity of liquid, since this would wash away the particles from the site of deposition.

Steiner does not disclose or suggest all of the elements of the claimed invention. Steiner does not disclose drug delivery systems suitable for nasal administration nor suggest a composition of microparticles having an average size between 10 and 20 microns. Steiner does not disclose or suggest modifying the particles for administration in a dry powder form to the nasal mucosa. Claims are not *prima facie* obvious if the primary references do not suggest all elements of the claimed invention and the prior art does not suggest the modifications that would bring the primary references into conformity with the application claims (*In re Fritch*, 23 U.S.P.Q.2d, 1780 (Fed. Cir. 1992). *In re Laskowski*, 871 F.2d 115 (Fed. Cir. 1989)). Thus Steiner does not provide the necessary motivation to one of ordinary skill in the art to modify its particles so that they are suitable for nasal administration. Therefore claims 1, 2, 4, 5, 7, 9, 12, 14, 15, 17, and 18 are not obvious over Steiner.

(iii) Rejection of claims 3, 8, 10, 16, 20, and 21 under 35 U.S.C. § 103(a) as being obvious over Steiner, in view of U.S. Patent No. 5,690,954 to Illum ("Illum").

**Steiner**

Steiner does not disclose antihistamines. Steiner does not disclose drug delivery devices for nasal administration. Steiner does not disclose spray drying. As mentioned above, Steiner

U.S.S.N.: 09/766,362  
Filed: January 19, 2001  
**APPEAL BRIEF**

does not disclose drug delivery systems suitable for nasal administration. Steiner does not mention nor suggest a composition of microparticles having an average size between 10 and 20 microns. Further, there is no suggestion in Steiner to modify the particles so that they can be administered in a dry powder form or any other form to the nasal mucosa.

**Illum**

Illum describes improving the bioavailability of high molecular weight drugs that are administered to the nasal cavity for systemic delivery (see col. 1, lines 15-18 and col. 4, lines 3-5). Illum addresses the problems of decreased efficiency of nasal drug delivery due to rapid clearance of nasal sprays and inefficient drug absorption in the nasal cavity by designing a bioadhesive microsphere delivery system that contains absorption enhancers. The bioadhesive microspheres adhere to the nasal mucosa upon contact by forming a gel (col. 3, lines 2-9) and have improved bioavailability due to the presence of absorption enhancers which increase the bioavailability of the drug (col. 4, lines 6-12). Illum discloses materials to increase bioavailability including lysophosphatides, phospholipids, and bile salts. Illum does not disclose or suggest the inclusion of dikeltopiperazines in the delivery system. Illum discloses microparticles with a size range between 10 and 100 microns (col. 6, lines 13-15). Illum does not suggest the selection of particles having a narrow size range of between 10 and 20 microns.

***The References in Combination***

Claims 3, 8, 10, and 16 are not obvious over Steiner in view of Illum. Neither Steiner nor Illum provides a person of ordinary skill in the art with the motivation to combine these

U.S.S.N.: 09/766,362  
Filed: January 19, 2001  
**APPEAL BRIEF**

references nor is there any indication of a reasonable likelihood of success. Steiner discloses oral or intravenous delivery of small microparticles having sizes ranging between 0.1 and 10 microns. In contrast, Illum is directed to particles with larger diameters, ranging between 10 and 100 microns, which may be administered to the nasal mucosa for drug delivery. Illum's microparticles are bioadhesive and form gels upon delivery to a mucosal surface (col. 6, lines 15-16). The MPEP explains that "[t]he mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combinations" (MPEP § 2143.01, quoting *In re Mills*, 916 F.2d 680, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990)). There is no disclosure or suggestion in Steiner to modify its particles so that they are larger (having an average size between 10 and 20 microns), and Illum does not suggest the selection of particles having a narrow size range between 10 and 20 microns. There is no suggestion in Steiner to modify its particles so that they can be administered in a dry powder form to the nasal mucosa. Furthermore, Illum does not suggest modifying its bioadhesive microparticles to include diketopiperazines and not require the formation of a gel. Thus Steiner and Illum do not provide the necessary motivation to one of ordinary skill in the art to combine these references because Steiner nor Illum suggest the desirability of the combination and do not provide a reasonable expectation of success. Indeed, Illum teaches away from what appellants' claim by teaching the criticality of a bioadhesive gel to obtain nasal delivery. Thus, one of ordinary skill in the art would not be motivated to combine Steiner with Illum. Even if one of ordinary skill in the art combined Steiner with Illum, claims 3, 8, 10, and 16 would not be

U.S.S.N.: 09/766,362  
Filed: January 19, 2001  
**APPEAL BRIEF**

obvious. Illum does not cure the deficiencies of Steiner. First, Illum discloses a broad range of diameters for the particles and does not suggest the selection of particles having a narrow size range of between 10 and 20 microns. Second, Illum discloses that microsphere delivery systems for drug delivery through the nasal mucosa must be both bioadhesive and contain absorption enhancers to increase the bioavailability of the drug to be delivered. In contrast, applicants have disclosed a different drug delivery system, one which requires the use of diketopiperazines and does not require the formation of a gel. There is no suggestion in Illum to modify the bioadhesive microparticles to include diketopiperazines and not require the formation of a gel. Thus, claims 3, 8, 10, and 16 would not be obvious over Steiner in view of Illum.

For the reasons discussed above, claims 20 and 21 would not be obvious over Steiner in view of Illum. Neither Steiner nor Illum disclose forming the microparticles by spray drying. Illum discloses forming microspheres by emulsion and phase separation methods, followed by chemical crosslinking (see col. 6, lines 22-67). Steiner discloses forming the microparticles via precipitation (see col. 9, line 55 until col. 10, line 9). Therefore the combination of Steiner with Illum would not make claims 20 and 21 obvious.

#### **(9) SUMMARY AND CONCLUSION**

Claims 1, 2, 4, 5, 7, 9, 12, 14, 15, 17, and 18 are not obvious over Steiner. Steiner does not disclose nor suggest all of the elements of the claimed invention. Steiner does not disclose or suggest drug delivery systems suitable for nasal administration, microparticles having an average size between 10 and 20 microns, or dry powder formulations. The formulations that are

U.S.S.N.: 09/766,362

Filed: January 19, 2001

**APPEAL BRIEF**

disclosed would not be suitable since they must be suspended in an aqueous medium for injection. Thus Steiner does not provide the necessary motivation to one of ordinary skill in the art to modify its particles so that they are suitable for nasal administration. Therefore claims 1, 2, 4, 5, 7, 9, 12, 14, 15, 17, and 18 are not obvious over Steiner.

Claims 3, 8, 10, 16, 20, and 21 are not obvious over Steiner in view of Illum. Neither Steiner nor Illum provides a person of ordinary skill in the art with the motivation to combine these references. There is no disclosure or suggestion in Steiner to modify its particles so that they are larger (having an average size between 10 and 20 microns) or so that they can be administered in a dry powder form to the nasal mucosa. There is no suggestion in Illum to select particles having a narrow size range between 10 and 20 microns or to modify its bioadhesive microparticles to include diketopiperazines and not require the formation of a gel. Thus Steiner and Illum do not provide the necessary motivation to one of ordinary skill in the art to combine these references. Therefore, claims 3, 8, 10, 16, 20, and 21 are not obvious over Steiner in view of Illum.

U.S.S.N.: 09/766,362  
Filed: January 19, 2001  
**APPEAL BRIEF**

For the foregoing reasons, Appellant submits that claims 1-5, 7-12, 14-18, 20 and 21 are patentable.

Respectfully submitted,



---

Patrea L. Pabst  
Reg. No. 31,284

Date: February 15, 2005

PABST PATENT GROUP LLP  
400 Colony Square, Suite 1200  
1201 Peachtree Street  
Atlanta, Georgia 30361  
(404) 879-2151  
(404) 879-2160 (Facsimile)

U.S.S.N.: 09/766,362  
Filed: January 19, 2001  
**APPEAL BRIEF**

#### **Appendix I: Claims On Appeal**

1. (previously presented) A composition for the nasal administration of a drug in a dry powder form suitable for administration to the nasal region,

the dry powder form comprising microparticles having an average particle size of between 10 and 20 microns and comprising the drug and diketopiperazines.

2. (original) The composition of claim 1 wherein the drug is selected from the group consisting of antihistamine, vasoconstrictors, antiinflammatories and analgesics.

3. (original) The composition of claim 2 wherein the antihistamine is selected from the group consisting of chlorpheniramine and azelastine.

4. (previously presented) The composition of claim 1 wherein the diketopiperazine is a substitution derivative selected from the group consisting of diketomorpholines, diketooxetanes and diketodioxanes.

5. (previously presented) The composition of claim 1 wherein the diketopiperazine diketopiperazine is formed by cyclodimerization of amino acid ester derivatives.

6. (canceled).

7. (previously presented) A drug delivery device for nasal administration comprising a drug in a dry powder form in a dosage formulation for administration to the nasal region, and

a device for delivering a measured dose of the drug to the nasal mucosa,

U.S.S.N.: 09/766,362  
Filed: January 19, 2001  
**APPEAL BRIEF**

wherein the dry powder form comprises microparticles having an average particle size of between 10 and 20 microns and comprising the drug and diketopiperazines.

8. (original) The device of claim 7 wherein the device is a nasal insufflator.
9. (original) The device of claim 7 wherein the drug is selected from the group consisting of antihistamine, vasoconstrictors, antiinflammatories and analgesics.
10. (original) The device of claim 7 wherein the antihistamine is selected from the group consisting of chlorpheniramine and azelastine.
11. (previously presented) The device of claim 7 wherein the diketopiperazine is a substitution derivative selected from the group consisting of diketomorpholines, diketooxetanes and diketodioxanes.
12. (currently amended) The device of claim 7 wherein the diketopiperazine diketopiperazine is formed by cyclodimerization of amino acid ester derivatives.
13. (canceled).
14. (previously presented) A method of administering a drug to the nasal region of a patient in need thereof, comprising nasally administering a dry powder suitable for nasal administration,  
wherein the dry powder form comprises microparticles having an average particle size of between 10 and 20 microns and comprising the drug and diketopiperazines.
15. (original) The method of claim 14 wherein the drug is selected from the group consisting of antihistamine, vasoconstrictors, antiinflammatories and analgesics.

U.S.S.N.: 09/766,362  
Filed: January 19, 2001  
**APPEAL BRIEF**

16. (original) The method of claim 14 wherein the antihistamine is selected from the group consisting of chlorpheniramine and azelastine.

17. (previously presented) The method of claim 14 wherein the diketopiperazine is a substitution derivative selected from the group consisting of diketomorpholines, diketooxetanes and diketodioxanes.

18. (previously presented) The method of claim 14 wherein the diketopiperazine diketopiperazine is formed by cyclodimerization of amino acid ester derivatives.

19. (canceled).

20. (previously presented) The composition of claim 1 formed by spray drying.

21. (previously presented) The device of claim 7 wherein the microparticles are formed by spray drying.

**TABLE OF CONTENTS**

- (1) REAL PARTY IN INTEREST**
- (2) RELATED APPEALS AND INTERFERENCES**
- (3) STATUS OF CLAIMS ON APPEAL**
- (4) STATUS OF AMENDMENTS**
- (5) SUMMARY OF THE INVENTION**
- (6) ISSUES ON APPEAL**
- (7) GROUPING OF CLAIMS**
- (8) ARGUMENTS**
  - (a) Rejections Under 35 U.S.C. § 103**
- (9) SUMMARY AND CONCLUSION**

Appendix I: Claims On Appeal

Table of Contents